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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/066,320 | 01/31/2002 | Jonathan S. Stamler | 1818.1030-003 | 1921 |

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| EXAMINER |
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GUPTA, ANISH

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| ART UNIT | PAPER NUMBER |
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1654

DATE MAILED: 06/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--------------------------------------|---------------------------------------|--|
| Office Action Summary | Application No. 10/066,320 | Applicant(s) STAMLER ET AL. | |
| | Examiner Anish Gupta | Art Unit 1654 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 March 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4-6 and 30-35 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4-6 and 30-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The amendment filed 3-3-06 is acknowledged. Claims 4-5 were amended. Claims 4-6 and 30-35 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 4-6 and 30-35 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons set forth in the previous office action and the reasons set forth below.

Applicant amended the claims to recite “under condition sufficient to preserve redox chemistry.” Applicants state that “[r]edox chemistry is well known in the art and refers to the transfer of NO from the heme Fe to cysteine in the β subunit with the loss of an electron.” Applicants state that the examples describe that high phosphate condition results in the predominant formation of methHb, low phosphate condition which preserve redox chemistry in hemoglobin result in predominant formation of SNOHb. See page 22-23 of the specification.

Applicants arguments have been fully considered but have not been found persuasive. Applicants have not fully enabled the claimed invention for the full scope of the claim. Applicants claims are drawn to “conditions” that allow the formation of S-nitrosohemoglobin. Applicants are

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yet again arguing the conditions of phosphate concentration. Applicant specification does not provide for all of the conditions necessary to achieve the desired result. Applicants have amended to recite that the conditions must preserve redox chemistry. However, the specification does not provide guidance what agents, temperature, or other conditions might affect redox chemistry. The only guidance provide is the concentration of the phosphate, see page 23, lines 6-13 of the specification. However, as stated in the previous office action, the results indicate that when 100 mM phosphate was used, formation of metHb was observed. Using 10mM phosphate shows the formation of iron nitrosyl Hb and some metHb. Using 10mM phosphate + borate resulted in predominantly iron nitrosylHb. Thus when phosphate is present in a concentration of 10mM the desired S-nitrosylHb is not obtained, rather Fe-nitrosylHb is obtained (see page 46 of Jia). Even where the phosphate concentration is in the range of 10 mM, much like the concentration claimed in claim 31, S-nitorosylHb is not obtained rather Fe-nitrosylHb is obtained. Clearly, “low concentrations” of phosphate is not enough to produce the desired product. Accordingly, specific conditions are necessary to make desired end product. The instant specification does not describe the all of the desired conditions to achieve S-nitrosohemoglobin. One would be burdened with undue experimentation in determining the appropriate conditions for obtaining S-nitrosylhemoglobin rather than obtaining methemoglobin or iron-nirtrosylhemoglobin.

Rejection is maintained.

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the

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mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can normally be reached on (571) 272-0562. The fax phone number of this group is (571)-273-8300.


Anish Gupta
Patent Examiner